SCN8A gene

sodium voltage-gated channel alpha subunit 8

Normal Function

The *SCN8A* gene belongs to a family of genes that provide instructions for making sodium channels. These channels allow positively charged sodium (Na) atoms (sodium ions) to pass into cells; they play a key role in a cell's ability to generate and transmit electrical signals.

The *SCN8A* gene provides instructions for making one part (the alpha subunit) of a sodium channel called $Na_v1.6$. The alpha subunit forms the hole (pore) in the cell membrane through which sodium ions flow. $Na_v1.6$ channels are primarily found in the nerve cells (neurons) of the brain and spinal cord (central nervous system) and neurons that connect the central nervous system to muscles and sensory cells that detect sensations such as touch, pain, heat, and sound (the peripheral nervous system). $Na_v1.6$ channels control the flow of sodium ions into cells, which makes it possible for neurons to communicate by generating and transmitting electrical signals.

Health Conditions Related to Genetic Changes

SCN8A-related epilepsy with encephalopathy

More than 100 mutations in the *SCN8A* gene have been found to cause *SCN8A*-related epilepsy with encephalopathy. This condition is characterized by recurrent seizures (epilepsy), abnormal brain function (encephalopathy), and intellectual disability. The signs and symptoms of this condition typically begin in infancy.

Most of these *SCN8A* gene mutations change a single protein building block (amino acid) in the $Na_v1.6$ channel. The mutations that cause *SCN8A*-related epilepsy with encephalopathy result in altered channels that stay open longer than usual, which increases the flow of sodium ions into neurons. The persistently open channels abnormally increase electrical signals, which can lead to excess activation (excitation) of neurons in the brain. This increased neuronal activity leads to seizures in people with *SCN8A*-related epilepsy with encephalopathy.

It is unknown how *SCN8A* gene mutations lead to intellectual disability, movement problems, and the other features of *SCN8A*-related epilepsy with encephalopathy. Because some affected children experience the loss of previously acquired skills (developmental regression) after the onset of seizures, it has been suggested that the seizures may impair brain function, but it is unclear if that is the case.

Lennox-Gastaut syndrome

Other disorders

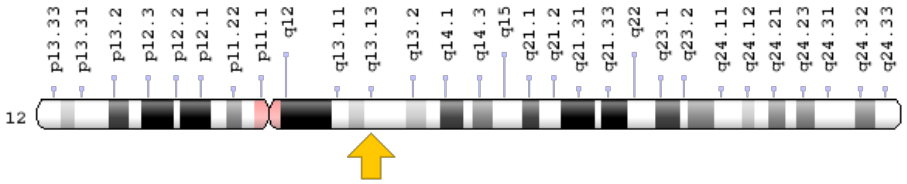
Mutations in the *SCN8A* gene have been found to cause intellectual disability and movement problems in some individuals. Unlike the mutations that cause *SCN8A*-related epilepsy with encephalopathy (described above), the *SCN8A* gene mutations that cause this condition result in the production of a $Na_v1.6$ sodium channel that is less active than normal, resulting in a decrease in the flow of sodium into neurons. This change does not increase neuronal signaling, so individuals with these mutations do not develop seizures. Researchers suspect that decreased neuronal signaling in the part of the brain that coordinates movement is the likely cause of the movement problems.

Other *SCN8A* gene mutations can cause movement problems and seizures called benign infantile seizures, which usually develop in the first year of life and stop by age 3. Unlike most other individuals with *SCN8A* gene mutations, these individuals have normal intellectual function. It is unknown why some *SCN8A* gene mutations cause these milder signs and symptoms while other mutations cause the more severe features of *SCN8A*-related epilepsy with encephalopathy.

Chromosomal Location

Cytogenetic Location: 12q13.13, which is the long (q) arm of chromosome 12 at position 13.13

Molecular Location: base pairs 51,591,233 to 51,812,864 on chromosome 12 (Homo sapiens Updated Annotation Release 109.20200522, GRCh38.p13) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- BFIS5
- CERIII
- CIAT
- hNa6/Scn8a voltage-gated sodium channel
- NaCh6
- Nav1.6

- sodium channel, voltage gated, type VIII, alpha subunit
- voltage-gated sodium channel subunit alpha Nav1.6
- voltage-gated sodium channel type VIII alpha protein

Additional Information & Resources

Educational Resources

- Jasper's Basic Mechanisms of the Epilepsies (fourth edition, 2012): Sodium Channel Mutations and Epilepsy
  https://www.ncbi.nlm.nih.gov/books/NBK98185/
- The Epilepsies: Seizures, Syndromes and Management (2005): Epileptic Encephalopathies in Infancy and Early Childhood in Which the Epileptiform Abnormalities May Contribute to Progressive Dysfunction
  https://www.ncbi.nlm.nih.gov/books/NBK2611/

Clinical Information from GeneReviews

- SCN8A-Related Epilepsy with Encephalopathy
  https://www.ncbi.nlm.nih.gov/books/NBK379665

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28SCN8A%5BTIAB%5D%29+OR+%28sodium+voltage-gated+channel+alpha+subunit+8%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- SODIUM CHANNEL, VOLTAGE-GATED, TYPE VIII, ALPHA SUBUNIT
  http://omim.org/entry/600702

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_SCN8A.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=SCN8A%5Bgene%5D
- HGNC Gene Symbol Report
  https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:10596
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:6334

- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/6334
- UniProt
  https://www.uniprot.org/uniprot/Q9UQD0

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Reviewed: August 2017
Published: June 23, 2020

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